

## **REMARKS**

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

Applicants respectfully request an interview in the case prior to issuance of any Official Action in order to expedite allowance of the application.

### **1. Status of the Claims**

As correctly noted in the Office Action Summary, Claims 1-7 and 12-28 are pending. Claims 12-28 are indicated withdrawn as directed to non-elected subject matter.

Upon entry of the above-listed amendments, Claims 5, 12-14, and 28 are canceled without prejudice of or disclaimer to the subject matter contained therein. Claims 1-4 and 6-7 will be indicated as pending, and Claims 15-27 will be indicated as allegedly withdrawn. Claims 1-4, 6-7, 15-18, 20-21, and 25-27 have been amended. Applicants submit in light of further comments provided below that withdrawn claims 15-27 in fact should be "pending" and not "withdrawn."

### **2. Response to Restriction Requirement**

Applicants agree with the assertion that the response to the Restriction Requirement was made *without* traverse.

Regarding the Office's assertion that claims 12-28 are withdrawn as being drawn to non-elected subject matter, Applicants disagree. The Restriction Requirement mailed May 14, 2003 (Paper No. 15) required the claims to be restricted to "DNA molecules encoding analogs of FGF molecules including (1) substitutions of amino acids 128-138, (2) deletions of the amino terminus spanning residues 1 to 24, and (3) combinations of substitutions and deletions." Office Action, p. 2. Applicants election Group I. No mention of claims 12-28 are made.

Applicants via this amendment have canceled claims 12-14 and 28 which are

directed to either non-elected subject matter or are rendered redundant given the amendment to Claim 1. The remaining claims relate to the elected group.

Applicants further note for the record that these remaining claims do not pose any additional search burden on the Examiner and are generally analogous to the claims which issued in the parent patent, U.S.P.N. 6,294,359. Accordingly, Applicants request that the reference as "withdrawn" to pending claims 15-27 be changed in the record to "pending".

**3. Acknowledgement of Information Disclosure Statements**

Applicants note receipt of the acknowledged 1449 form submitted October 5, 2001 with thanks.

**4. Priority**

The Office Action notes "that the instant application has an extensive patent application history, with a number of continuation-in-part applications. A review of some of the patent applications in the patent family indicate that priority for the claimed subject matter (bFGF analogs which comprise substitutions in the region of amino acids 128-138) reaches at least back to U.S. Pat. Application No. 07/459,739 (02/12/90), but not back to 06/809,163 (filed 12/16/95). Art will be applied according to this date."

Applicants first note that 06/809,163 (now USPN 5,439,818) was filed December 16, 1985, not 1995. Applicants further note that the present Application is a divisional application of U.S. Patent Application No. 09/098,628, now U.S. Patent No. 6,294,359, filed June 16, 1998, which is a divisional application of U.S. Patent Application No. 07/459,739, now U.S. Patent No. 5,859,208, filed on February 12, 1990, which is a continuation-in-part application of U.S. Patent Application No. 07/070,797, filed July 7, 1987, now abandoned, which is a continuation-in-part application of U.S. Patent Application No. 07/050,706, filed May 15, 1987, now abandoned, which is a continuation-in-part application of U.S. Patent Application No. 06/869,382 filed May 30, 1986, now abandoned, which is a continuation-in-part

application of U.S. Patent Application No. 06/809,163, now U.S. Patent No. 5,439,818, filed December 16, 1985, which is a continuation-in-part application of U.S. Patent Application No. 06/775,521, filed September 12, 1985, now abandoned.

Applicants also disagree with the Office regarding priority. Claims 1-7 of the present invention are fully supported by the specification of U.S. Patent Application No. 07/070,797, filed July 7, 1987. For example, Example 5 of U.S. Patent Application No. 07/070,797 discloses the preparation of many human basic FGFs in which one or more of the four cysteine residues were replaced with serine. These basic FGFs were prepared by site-specific mutagenesis of bFGF DNA, these are listed in Table 1 page 50 of the specification of U.S. Patent Application No. 07/070,797). It was also disclosed that all of these substituents resulted in the recovery of active FGF protein (see *e.g.*, page 49, lines 2-3 of the specification of U.S. Patent Application No. 07/070,797). Another FGF protein (Proline to Serine conversion at position 128) is also supported by the U.S.S.N. 06/809,163, now U.S.P.N. 5,439,818, which was filed December 16, 1985. See Example 7 of the '818 patent.

#### **5. Claim Objections**

Claims 1-7 are objected to for purportedly reciting non-elected subject matter. The claims are amended herein to recite the elected subject matter, *i.e.*, to substitutions in the region of 128-138 of bFGF. Thus, the objection is mooted.

#### **6. Rejections Under 35 U.S.C. § 101**

Claims 1-7 stand rejected under 35 U.S.C. § 101, because the claimed invention is purportedly directed to non-statutory subject matter. Specifically, the Examiner states that the phrase "DNA sequence" is not statutory subject matter. As suggested by the Examiner, claims 1-7 are amended herein to recite "DNA molecule". Applicants have also amended claims 15-27 to also recite the term. Thus, the rejection is obviated.

Claims 1-7 stand further rejected, because the claims purportedly recite a product of nature. The Examiner argues that the recitation of "recombinant" does not distinguish the claimed DNA from a DNA which would be found in nature because all DNA is recombinant. The claims are amended herein to recite "isolated DNA molecules", as suggested by the Examiner and in order to expedite prosecution of the application. Support for the term "isolated" can be found in the specification at least at page 11; page 30, lines 5-7; and the original claims. The skilled artisan would readily have understood at the time that "DNA sequence" as used in the specification refers to the molecule encoding the respective polypeptide. Thus, this rejection is obviated.

For the record, Applicants point out that it would have been understood in the art at the time what was meant by the word "recombinant" as well as today. Applicants have amended the phrase at the suggestion of the Examiner, but do not acquiesce to the argument that "recombinant" does not distinguish the claimed DNA from a DNA which would be found in nature. For example, recently issued U.S.P.N. 6,803,213 recites the phrase "recombinant DNA molecule" within the body of several of the claims. A reading of Applicants' specification would make readily apparent that the claimed DNA moiety is one that is produced by "the hand of man".

**7. Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-3 stand rejected as purportedly indefinite, for the recitation of the term "analog". The Examiner argues that the recitation of "analog" without a recitation of function implies any DNA sequence encoding something that differs from "mammalian FGF".

Applicants traverse the rejection. However, for purposes of advancing prosecution, Applicants have deleted the term from the claims, thereby mooted the rejections. Applicants respectfully request allowance of the claims.

**8. Rejections Under 35 U.S.C. § 112, First Paragraph**

Claims 1-4 stand rejected under 35 U.S.C. § 112, first paragraph, because

the specification, while being enabling for an isolated DNA encoding human basic FGF having a reduced affinity for heparin binding wherein the protein comprises a substitution of a positively charged amino acid residue within the region of amino acids 128-138 with a neutral or negatively charged amino acid, purportedly fails to provide enablement for any bFGF protein with reduced affinity for heparin binding.

The claims are amended herein to recite an isolated DNA molecule encoding human basic FGF having a reduced affinity for heparin binding, wherein the protein is substituted at residues within the region of amino acids 128-138. In light of the above comments, and in light of the amendments made herein, Applicants request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

**9. Rejections Under 35 U.S.C. § 102**

Claims 1-4 are rejected under 35 U.S.C. § 102(b) as being anticipated by Baird et al. (*Rec. Prog. Horm. Res.* 42: 143-205, 1986). Baird et al. purportedly disclose a number of analogs of bFGF, including peptides of bFGF. The Examiner states that "[b]ecause some of the peptides lack the heparin binding domain of amino acids 128-138, these peptides would also possess a reduced affinity for heparin binding."

Applicants traverse the rejection. Applicants submit that the cited references fail to recite every element of the presently claimed invention as amended. To anticipate a claim, a single prior art reference must teach each and every element of the claimed invention. See e.g., M.P.E.P. § 2131; *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986). The claims as amended recite a mammalian FGF molecule that comprises substituting one or more positively charged amino acid residues located in a heparin binding domain of residues 128 through 138 with a neutral or negatively charged amino acid. The reference does not teach or suggest such a substitution. Accordingly, the reference fails to teach or suggest the claimed invention as

amended.

Applicants also respectfully point out that they have priority back to 1985, as discussed *supra*. Thus, the cited reference is not prior art under 35 U.S.C. § 102. Applicants respectfully request withdrawal of the rejection in view of the claim amendments and argumentation provided.


### **CONCLUSION**

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. 02-4800.

Respectfully submitted,  
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